Assessing and Managing Asymptomatic Ventricular Preexcitation in the Young Athlete

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PATIENT BACKGROUND

Mr E is a 22-year-old college hockey player. Major features of his past medical history include right-sided necrotizing pneumonia requiring chest tube placement at age 15, a concussion sustained while playing ice hockey at age 19, and patellar dislocation at age 21. On October 25, 2020, he developed new onset upper respiratory symptoms possibly as a result of becoming infected with SARS-CoV-2, the pathogen causing COVID-19. This prompted the need for a clinical evaluation by his primary care physician, including undergoing testing for COVID-19, which returned negative.

Initial cardiac-specific testing carried out during Mr E's primary care clinical evaluation included a resting 12-lead electrocardiogram (ECG) study, which revealed a normal sinus rhythm but with delta waves (Figure 1) consistent with ventricular preexcitation. This observation prompted a referral to cardiology where it could be viewed on follow-up serial ECG studies that he continued to demonstrate normal sinus rhythm and delta waves, as previously noted. His respiratory rate, blood pressure, and pulse readings consistently remained within normal limits, and normal cardiac structure and function could be observed on transthoracic echocardiographic testing. Prior to the present cardiology workup, he also endorsed no history of an underlying arrhythmia or related symptoms of lightheadedness, presyncope, syncope, or palpitations, and he could not recall any family history of cardiac conditions, such as coronary artery disease, heart failure, arrhythmias, or unexplained death at a young age. Results from laboratory blood panel testing for complete blood counts and chemistries also returned normal.

Because of the nature of Mr E's clinical cardiology referral, his workup included a cardiopulmonary exercise test (CPET) to better assess accessory pathway (AP) conduction. Because of his resting preexcitation ECG pattern, specific choices made for his CPET included the use of a stationary upright cycle in order to minimize motion artifact and changing the ECG paper sweep speed from 25 to 50 $mm \cdot s^{-1}$ to work together to enhance the visualization of the ECG tracing and optimize the diagnostic yield of the test.

The patient provided a maximal physiological effort CPET indicated by a peak exercise respiratory exchange ratio of 1.17. He achieved a peak heart rate of 185 $b \cdot min^{-1}$ and peak exercise oxygen uptake ($\dot{V}o_2$) of 32.1 $mL \cdot kg^{-1} \cdot min^{-1}$, amounting to 93% and 90% of predicted values, respectively. Notable features of his exercise ECG included PR interval prolongation, but without complete loss of delta waves (Figures 2 and 3). An abrupt loss of the delta wave from one heartbeat to another would have been consistent with a lower-risk AP.

After completing CPET the patient followed up with an electrophysiologist, who determined a high-risk pathway could not be definitively excluded. An invasive electrophysiology study (EPS) confirmed the presence of ventricular preexcitation, although falling within the low-risk category. This could be primarily attributed to an AP effective refractory period of 430 milliseconds (ms) while incrementally pacing the right atrium at a cycle length of 700 ms (85 $b \cdot min^{-1}$), and an atrioventricular (AV) node effective refractory period of 260 ms while pacing at 700 ms. The patient did not require medically necessary catheter ablation of the pathway, and he received unconditional medical clearance to return to competitive sport participation.

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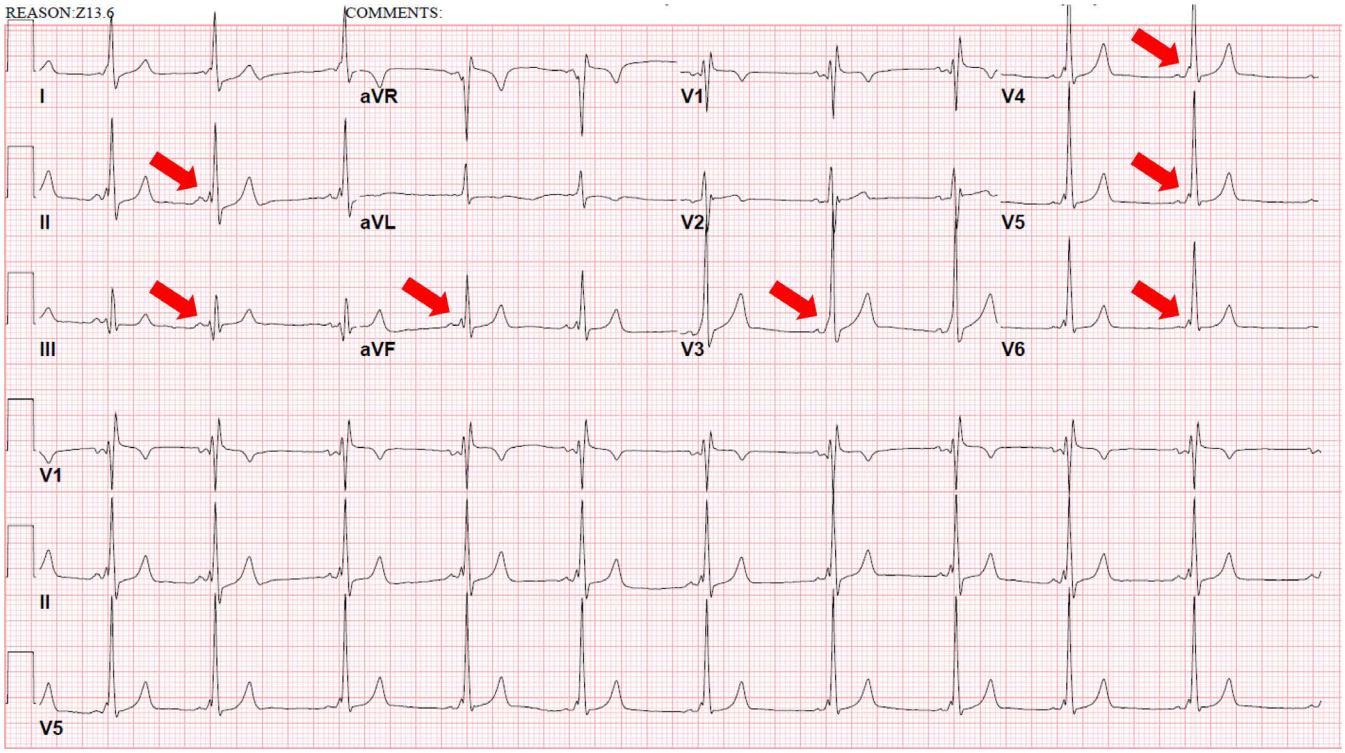

FIGURE 1. Initial ECG showing presence of preexcitation and delta waves (red arrows), most prominent in the inferior and precordial leads.

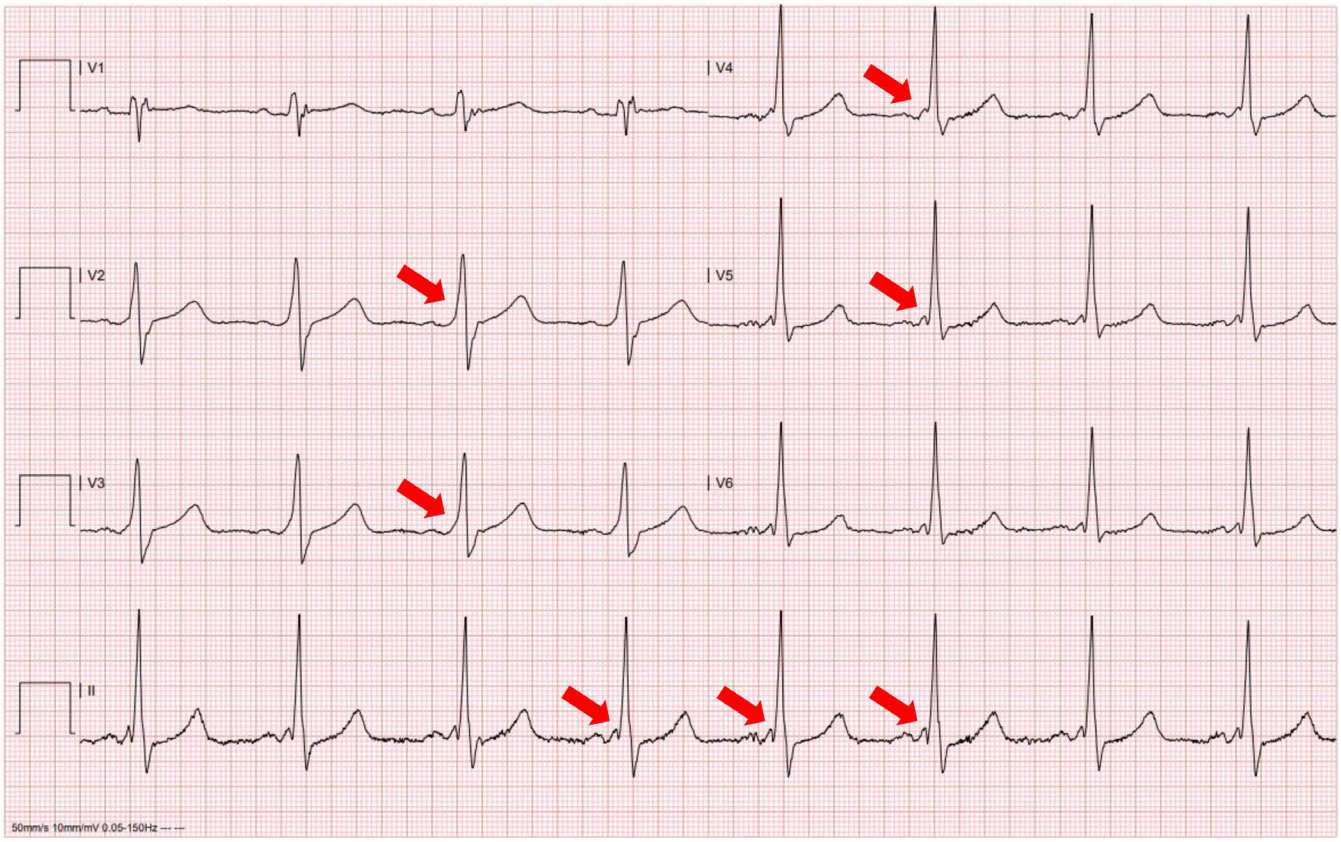

FIGURE 2. Exercise ECG obtained 1 min into exercise on supine bike at a heart rate of 95 b·min^{-1}. Sweep speed has been increased from 25 mm·s^{-1} to 50 mm·s^{-1} to better illustrate delta waves which remain visible (red arrows).

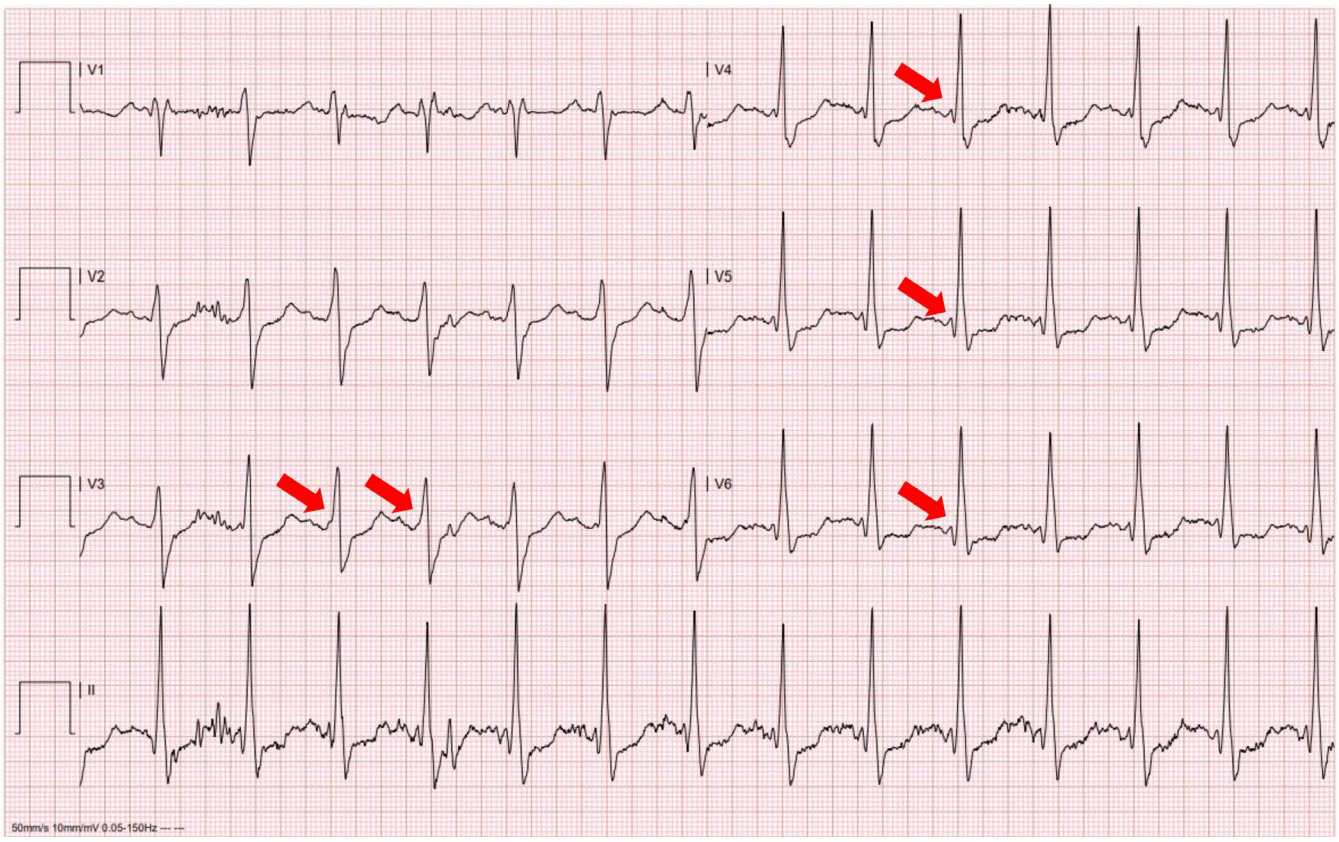

FIGURE 3. Exercise ECG obtained at peak exercise, 11 min into exercise at a heart rate of 169 b·min^{-1}. Again, delta waves remain visible (red arrows).

DISCUSSION

Etiology and Epidemiology

In a structurally normal heart in sinus rhythm, depolarization of the atrium starts in the sinoatrial node and eventually proceeds to the AV node. Following AV node conduction, the His-Purkinje system plays a major role in proper ventricular depolarization and early depolarization of the ventricles before the AV node is prevented by the naturally electrical-resistant cardiac tissue surrounding the AV node (1). This structural area of the heart electrically isolates the atria from the ventricles, except at the site of penetration of the AV conducting system (1,2).

Ventricular preexcitation is a condition where electrically conductive fibers, known as bundles of Kent or APs, connect the atrium to the ventricle outside of the AV node, bypassing the electrically conductive-resistant cardiac tissue (3). This results in partial ventricular activation earlier than would be expected if conduction occurred solely through the AV node. The hallmark features of preexcitation viewable on a 12-lead ECG include: (a) PR interval less than 120 ms (0.12 sec) during sinus rhythm, (b) QRS complex duration exceeding 120 ms, and (c) a slurred, slowly rising upstroke or downstroke of the QRS complex (known as a delta wave) (4).

A recent study that reviewed 300,000 ECGs reported the incidence of preexcitation in the general population is approximately 0.9 per 1,000 ECGs (5), which is consistent with that reported in previous large-scale studies (6,7). Overall, long-term development of atrial fibrillation and heart failure are more common in patients with preexcitation than in those without preexcitation (5). Importantly, when patients with ventricular preexcitation endorse symptoms such as palpitations or syncope, or develop an arrhythmia, this is commonly referred to as Wolff-Parkinson-White (WPW) syndrome. The peak incidence of WPW has been reported in adults between the ages of 30 to 40 y, and the prevalence may be higher in males than females (8,9). A major concern is that these patients are at an elevated risk for the development of tachyarrhythmias, increasing the likelihood of progression to life-threatening heart failure or sudden cardiac death (SCD). The classical presentation of these arrhythmias is reciprocating (reentrant) tachycardia with anterograde, or forward, conduction over the AV node; and retrograde, or backward, conduction involving the AP, also known as orthodromic atrioventricular reentrant tachycardia (AVRT) (3).

The most critical complication of ventricular preexcitation is development of ventricular fibrillation and subsequent SCD (10,11). This occurs in patients with WPW who enter atrial fibrillation or orthodromic atrioventricular reentrant tachycardia with rapid conduction down the AP causing rhythm degradation and ventricular fibrillation (11). Overall, it is estimated patients with WPW have an approximately 4% lifetime risk of SCD related to their WPW, which is higher than the general population (12).

Clinical Manifestations

Although some patients with a preexcitation pattern on ECG will be asymptomatic, most will demonstrate an episodic pattern of symptoms. This is consistent with studies of patients demonstrating preexcitation patterns on resting ECG where 64% endorsed symptoms at presentation and 20% developed symptoms at follow-up (13,14), generally reported as palpitations, chest pain, and syncope in 22%, 5%, and 4% of cases, respectively, whereas 38% of patients had a known history of supraventricular tachycardia, 0.4% had atrial fibrillation, and SCD occurred in 0.2% of cases.

Alternatively, others have reported that of patients who experience a life-threatening event, paroxysmal atrial fibrillation occurred in approximately 50% of cases (15). Further complicating the understanding of how symptoms translate to clinical implications, up to 55% of patients with all forms of supraventricular tachycardia are initially diagnosed with a panic disorder (16). This may in certain instances delay proper diagnosis, which may place certain individuals at an increased risk of SCD (16). However, it has been determined based on a 10-year review of cases of NCAA athletes that in general ventricular preexcitation is an uncommon culprit for SCD in these individuals, accounting for only 3% of all cardiac causes of death (17); although, this prevalence may be an underestimate due to lack of wide-spread and standardized ECG screening and a large number of cases without a clear identifiable cause.

Diagnosis and Risk Stratification

Diagnosis of preexcitation is concluded from a 12-lead ECG study meeting the criteria outlined above. Once identified, it is recommended that a full medical history, laboratory blood panel testing for counts and biochemistry, thyroid function, and transthoracic echocardiographic studies be performed to evaluate the individual for possible congenital or structural heart abnormalities (18). Although asymptomatic preexcitation cases tend to yield a less-severe clinical course than symptomatic cases, assessing risk is important in all instances, particularly in competitive athletes and those in high-risk occupations (13,18).

The hallmark feature of risk stratification involves the assessment of the pathway's refractoriness, or how effectively it can conduct at faster heart rates. Patients exhibiting short AP refractoriness, or the ability to conduct at faster heart rates, demonstrate a higher risk of SCD and should receive treatment (8,18). Alternatively, if there is a sudden prolongation of the PR interval with abrupt loss of the delta wave from one beat to another, this suggests the AP has a long refractory period and therefore is lower-risk for perpetuating tachyarrhythmias and adverse cardiac events (19). Nevertheless, more recent literature and the most recent 2019 European Society of Cardiology Guidelines are in favor of earlier invasive risk assessment with an EPS involving cases of asymptomatic preexcitation, particularly in athletes (18, 20–23).

During an EPS, the effective refractory period of the AP can be directly measured. When the effective refractory period is less than 250 ms, this is highly suggestive of a high-risk pathway requiring the patient to strongly consider undergoing ablation (8,18). Additional high-risk features observed during an EPS are inducibility of orthodromic atrioventricular reentrant tachycardia or the presence of multiple APs (18).

Treatment

If patients diagnosed with asymptomatic preexcitation are observed to exhibit high-risk features, catheter ablation of the pathway should be strongly considered (18). Pharmacological therapy should be implemented only for those unable or unwilling to undergo ablation (18). At experienced centers, catheter ablation therapy has a high success rate (>95%) while carrying a very low risk of major complications (8,24,25). For example, a study randomized high-risk patients with preexcitation to catheter ablation versus no intervention with 5 year follow-up. The intervention group saw a dramatic decrease in arrhythmic events over the follow-up period (7% vs 77%, $P < 0.001$) (25).

Due in part to the improved success of catheter ablation therapy, and concerns that some high-risk patients may be missed despite invasive risk assessment with an EPS, some experts advocate for ablation therapy for those even determined to be at low risk of SCD. This treatment plan may be particularly relevant if left ventricular dysfunction is noted on the echocardiogram (15,18). Regardless of treatment strategy, patients should regularly follow up with a cardiologist to assess for occurrence or recurrence of symptoms (18).

CLINICAL EXERCISE IMPLICATIONS

Exercise Testing

Exercise testing is an established risk-assessment tool for patients exhibiting a preexcitation ECG pattern (26). Relative to an EPS, exercise testing with ECG monitoring is low cost, more readily available at most centers, and is generally considered a low-risk and safe procedure. The selection of upright cycle ergometry is also the preferred modality when there is a particular need to identify details on the ECG tracing. Treadmill testing can reduce ECG quality due to motion artifact, making rhythm interpretation challenging. Additionally, changing the ECG paper speed from 25 to 50 $mm \cdot s^{-1}$ may be useful for enhancing the visualization of the ECG tracing and identifying delta waves. Collectively, incorporating these features into exercise testing can help to improve the diagnostic yield from acquired data.

When patients undergo noninvasive testing for the evaluation of ventricular preexcitation, careful interpretation of the ECG is paramount. Gradual loss of the delta wave with exercise is not accepted as specific for a long-refractory period and should not be used to label an AP low risk. Ultimately the gold standard for risk assessment is an invasive EPS and should be pursued in patients with symptoms, or in asymptomatic patients if the AP cannot clearly be identified as low risk via exercise testing.

Exercise Participation

Limited data exists on the effect of exercise on patients with untreated asymptomatic or symptomatic preexcitation. However, it is a generally accepted practice to withhold patients identified with this condition from sports and intensive exercise until the AP is further evaluated, risk stratified, and treated, as needed. Although noninvasive exercise testing is useful for screening most individuals where known or unknown ventricular preexcitation may be present, for athletes and other adults in high-risk professions an invasive EPS with or without ablation may be recommended before the individual is allowed to return to play or work without restriction (18). The long-term success rate associated with treating individuals diagnosed with exhibiting ventricular preexcitation patterns using AP ablation is nearly 95%, with a less than 1% risk of procedural complications. On the other hand, it should be emphasized that all patients with a history of ventricular preexcitation require lifelong annual follow-up consultations with a cardiologist because these individuals are at higher risk for development of symptoms and arrhythmias (19).

SUMMARY

Athletes who exhibit asymptomatic ventricular preexcitation patterns on a 12-lead ECG study should be temporarily removed from intensive exercise and competition until further clinical cardiology and EP testing can be completed. The major goal for clinicians is to risk-stratify patients based on the combination of signs and symptoms, and if necessary, offer advanced treatment options to individuals with the ultimate goal of allowing for the safe and unconditional return to training and competition. While a well-conducted exercise testing plays an important role in the risk assessment process, it is also not rare for individuals to be asked to undergo risk-stratification via an invasive EPS, possibly followed by a catheter ablation procedure to treat the affected area. After treatment or verification they are at low-risk for adverse cardiac events, athletes may return to competition while also adhering to routine annual follow-up in cardiology.

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